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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,187	07/30/2003	Jurgen Engel	ZEN-015-NP	9817

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GOODWIN PROCTER LLP
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EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
04/27/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/632,187	ENGEL ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/3/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments filed 3/3/11 have been fully considered but they are not deemed to be persuasive.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 4 and 12 are pending in this office action.

4. The information disclosure statement (IDS) submitted on 3/3/11 is acknowledged and has been reviewed.

5. The rejection of claims 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn based on cancellation of the claims 1 and 3.

Maintained Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nickel et al. (US Patent 6,696,428) and Hilgard et al. (1993) in view of Stekar et al. (1995) and Goodman and Gilman (all previously made of record) for the reasons made of record and as follows.

Nickel et al. teach anti-tumor compounds such as miltefosine or octadecyl (1,1-dimethylpiperidinio-4-yl) phosphate (i.e., perifosine), wherein said compounds are used

in pharmaceutical compositions or dose units (i.e. drug products) for effective treatment of cancer (see col. 1, lines 10-17; col. 2, lines 40-44; claim 12).

However Nickel fails to teach treating mammary cancer and also fails to teach that the treatment requires an antimetabolite (such as 5-fluorouracil, fludarabin, gemcitabin and cytarabin).

Hilgard teach an analog of perifosine (i.e., miltefosin, an alkyphosphocholine compound) for the treatment of mammary carcinoma (see pg 91 under activity of miltefosine) in combination with cisplatin (see pg 93).

However Hilgard fails to teach the structural compound of formula II of instant claim 1 and the specific antimetabolites recited.

Stekar et al. teach the drug miltefosine is administered before or prior to the. administration of cyclophophamide (see page 373, rt. col. as in claims 4 and 12).

However Skekar fails to teach the use the octadecyl (1,1- dimethylpiperidinio-4-yl) phosphate (i.e., perifosine) as required by instant claim 12 compound formula II.

One of ordinary skill in the art would have been motivated to expand or broaden the generic treatment method of cancers as taught by Nickel to include treating mammalian cancers as taught by Hilgard, and to substitute Hilgard's drug miltefosin for perifosin with a reasonable expectation of success because both drugs are functionally equivalent as taught by Nickel.

Goodman et al. disclose in Table X-1, a list of known anti-tumor agents, such as 5-fluorouracil or cyclophosphamide etc., for treating mammary carcinomas or tumors of mammary origins.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the methods of both Nickel et al. by additionally administering the anti-tumor agents disclosed by Calabresi/Goodman et al. because one of ordinary skill in the art would reasonably expect the combined properties of the anti-tumor compounds to effectively treat patients suffering from tumors or various cancer. Moreover, Calabresi/Goodman et al. teach that drugs are generally more effective in combination therapy and may provide synergistic effect through biochemical interactions.

Thus, the claimed invention would be prima facie obvious to at the time of filing.

Applicant again argues that a person of skill would not have reasonably expected the claimed combination of perifosine and the cited antimetabolites to be more effective or synnergistic for the treatment of mammary carcinoma. Specifically Applicant states that as detailed in the 1984 Chau and Talalay drug combination may be additive or antagonistic. Additionally Applicant asserts that because these mechanisms of action are different a person of ordinary skill in the art would not have recognized that sensitivity and or resistance of a particular cancer to cyclophoshamide would be different.

In Response Applicant's argument have been considered but found not persuasive because the same fact that applicant is relying on (i.e., different mechanism of the agents) is taught by Goodman and Gilman (already of record) which teaches that drugs are generally more effective in combination and may be synergistic through biochemical interactions. Further teaching that it is more effective to use drugs that do

not share common mechanism... see page 1230, 3rd para. Based on the teachings contrary to Applicant's assertion one of ordinary skill in the art would have been motivated to employ drugs which are based on the different mechanism of action to treat the same type of cancer. Therefore Applicant's argument is what is already known in the prior art.

Maintained Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims **4 and 12** stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-19** of U.S. Patent Application No. **12751608**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

- • The claims of the instant application '187 refer to treating mammalian cancer comprising administration of an alkylphosphocholine of compound of formula II with an antimetabolite (see claim 12) and the copending application '608 refers to use of a formulation of an alkylphosphocholine in combination of an antimetabolite for the treatment of cancer.

- • Both applications recite using the same compositions and/or derivatives thereof. See current application claims 4 and 12 and copending application claims 1-19. The compositions recited in the claims are anticipatory of each other.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

8. Claims **4 and 12** stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-14** of U.S. Patent Application No. **12751454**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

- • The claims of the instant application '187 refer to treating mammalian cancer comprising administration of an alkylphosphocholine of compound of formula II with an antimetabolite and the copending application '454 refers to treating oncogenesis/cancers generically with a formulation of an

alkylphosphocholine in combination of an antimetabolite for the treatment of cancer.

- • Both applications recite using the same compositions and/or derivatives thereof. See current application claims 4 and 12 and copending application claims 1-14. The compositions recited in the claims are anticipatory of each other.
- One of ordinary skill in the art would have been motivated to use the generic treatment of cancers recited by the copending application to treat specific cancers such as mammalian cancers recited in the instant application with a reasonable expectation of success.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Applicant request that the double patenting rejection be made in the copending rejection since the double patenting rejection will be the only remaining rejection.

In response, since this is not the only rejection remaining the double patenting rejection is maintained.

9. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1628
4/18/11

/Brandon J Fetterolf/
Supervisory Patent Examiner, Art Unit 1628